

October 20, 1948.

Dr. Wilton S. Stone,
Dept. Zoology,
University of Texas,
Austin, Texas.

Dear Dr. Stone,

You may have heard about this already, but if you haven't I thought you'd like to hear about some of our recent work with *E. coli*.

Most important, a still murky situation- the production of persistent heterozygotes in crosses with some strains. While doing some routine phage-resistance inheritance studies, I noticed a prototroph which was Lac⁺ on synthetic FMB, but showed ⁺/₋, -, and mosaic colonies on a complete Lac FMB. It turned out to be segregating for other nutritional and phage resistance characters also, and showed a large number of crossover types among the segregants. It can be maintained on synthetic medium only, where it can compete with the segregants, most of which have various nutritional deficiencies; on complete medium it rapidly segregates out. These segregants were tested to determine whether they would reproduce this phenomenon in crosses, and they did so, about 10% of the Lac⁺ prototrophs formed being heterozygous for Lac⁺ / Lac⁻. However, there is an aberration somewhere: Mal is regularly hemizygous, and factors in the neighborhood of Mal do not segregate at random from their heterozygotes, but are strongly distorted. I would conclude tentatively that there is a recessive lethal deficiency for a segment of one of the chromosomes, including Mal, which is responsible for the distortion. I can't account for the way in which the deficiency is produced, nor why such heterozygotes persist in contrast to the typical behavior. The factor, whatever it is, which is transmitted to the segregants, is as effective when present in both as in one of the parents, and is not likely to be an inversion. I haven't mapped these factors yet, but the observation that all of the heterozygotes have been non-segregating Galactose⁺ and Arabinose⁺, although one of the parents carried - alleles, may be a lead, and possibly in the direction of a crossing-over interpretation. Single-cell and cytological studies are in a late stage of planning. Although the heterozygous cells are perhaps a little longer than the typical (and I haven't studied them very carefully yet), they are not in any sense filaments. However, the initial zygote might be very different morphologically from these derived diploids. A careful reexamination of Lac⁺ prototrophs from standard stocks, using very favorable material- closely linked Lac₁⁻ and Lac₂⁻ in repulsion, indicated nothing like this in that material. However, knowing how to look for it now, I hope to be able to induce situations where non-aberrant heterozygotes may be found. Some of this work is being written up now, and should be published before too much longer.

With best regards,

Yours sincerely,

Joshua Lederberg